

IN THE CLAIMS

Please cancel claims 18, 19, 38, 40, 43 and 44 without prejudice, and amend claim 17 as follows:

1.-16. (CANCELED)

17. (CURRENTLY AMENDED) A method for replacing a target fragment of a gene in a cell in vivo, the method comprising delivering to the cell an exogenous replacement DNA fragment, the replacement DNA fragment consisting of:

- (a) at least one replacement exon having a 3' end and a 5' end;
- (b) a 3' end consisting of a 3' flanking noncoding sequence adjacent to the 3' end of the at least one replacement exon; and
- (c) a 5' end consisting of a 5' flanking noncoding sequence adjacent to the 5' end of the at least one replacement exon;

wherein the replacement DNA fragment is from 1 to about 2000 bases and includes less than all of the exons of the gene, and wherein the 3' flanking noncoding sequence of the replacement DNA fragment is homologous to and anneals to a 3' flanking noncoding sequence adjacent to the target fragment, and the 5' flanking noncoding sequence of the replacement DNA fragment is homologous to and anneals to a 5' flanking noncoding sequence adjacent to the target fragment, so that the exogenous replacement DNA fragment replaces the target fragment of the gene in the cell, wherein the DNA is delivered into the cell by microinjection or electroporation, or by local direct administration of a lipid-DNA complex comprising the replacement DNA fragment.

18.-19. (CANCELED)

20. (PREVIOUSLY PRESENTED) The method of claim 17, wherein the target fragment of the gene in the cell comprises a DNA sequence comprising a genetic defect associated with a disease or dysfunction.

21. (PREVIOUSLY PRESENTED) The method of claim 20, wherein the disease or dysfunction is Fanconi's anemia, cystic fibrosis, sickle cell anemia, thalassaemias, retinitis

pigmentosa, xeroderma pigmentosum, ataxia telangiectasia, Bloom's syndrome, retinoblastoma, Duchenne's muscular dystrophy, Lesch Nyhan syndrome, adenosine deaminase deficiency or Tay-Sachs disease.

22. (PREVIOUSLY PRESENTED) The method of claim 20, wherein the target fragment of the gene is a DNA sequence present in the cystic fibrosis gene.

23. (PREVIOUSLY PRESENTED) The method of claim 20, wherein the target fragment of the gene is a DNA sequence present in the sickle cell anemia gene and the target fragment is replaced with a replacement genomic DNA sequence encoding a region of β -globin.

24. (PREVIOUSLY PRESENTED) The method of claim 20, wherein the target fragment of the gene is a DNA sequence present in the gene causing thalassaemias, wherein the sequence is replaced with a replacement genomic DNA sequence in the thalassaemias causing genomic loci.

25. (PREVIOUSLY PRESENTED) The method of claim 20, wherein the target fragment of the gene is a DNA sequence present in a gene causing xeroderma pigmentosum.

26. (PREVIOUSLY PRESENTED) The method of claim 17, wherein the replacement DNA fragment is single stranded.

27. (PREVIOUSLY PRESENTED) The method of claim 17, wherein the replacement DNA fragment is double stranded.

28. (PREVIOUSLY PRESENTED) The method of claim 17, wherein the delivering of the exogenous replacement DNA fragment comprises delivery by electroporation, microinjection, complexing the exogenous replacement DNA fragment in a lipid layer, complexing the exogenous replacement DNA fragment in a cationic lipid, complexing the exogenous replacement DNA fragment in a dendrimer or conjugating the exogenous replacement DNA fragment to polylysine.

29. (PREVIOUSLY PRESENTED) The method of claim 17, wherein the method is carried out in a population of cells containing the target fragment of the gene, and further comprising determining the extent of homologous replacement by identification of cells within the population that have replaced the target fragment of the gene with the exogenous replacement DNA fragment at a target genomic locus, wherein the identification comprises PCR or Southern hybridization.

30. (PREVIOUSLY PRESENTED) The method of claim 29, wherein the exogenous replacement DNA fragment is identified using primers of about 25 bases that are outside of regions of homology defined by the exogenous replacement DNA fragment, or primers that are allele-specific and differentiate between the target fragment of the gene and the exogenous replacement DNA fragment, or by Southern hybridization with allele-specific oligonucleotide probes that differentiate between the target fragment of a gene and the exogenous replacement DNA fragment.

31. (PREVIOUSLY PRESENTED) The method of claim 17, wherein the exogenous replacement DNA fragment is uncoated or coated with a recombinase or complexed with a protein, provided that the recombinase is not recA.

32. (PREVIOUSLY PRESENTED) The method of claim 17, wherein the exogenous replacement DNA fragment is generated by PCR amplification, oligonucleotide synthesis, plasmid cleavage with restriction endonuclease or by a combination of restriction enzyme cleavage of plasmid inserts and ligation of contiguous insert fragments.

33. (PREVIOUSLY PRESENTED) The method of claim 32, wherein the PCR amplification is performed with primers specific for the exogenous replacement DNA fragment.

34. (PREVIOUSLY PRESENTED) The method of claim 33, wherein the target fragment of a gene is a DNA sequence present in the cystic fibrosis gene, and the primers are selected from the group consisting of primers CF1, CF1B, CF5, CF6, CF7B, CF8B, CF7C, CF8C, CF9, CF14, CF17 and CF22.

35. (PREVIOUSLY PRESENTED) The method of claim 33, wherein the target fragment of a gene is a DNA sequence present in the sickle cell anemia gene, the target fragment is replaced with a replacement genomic DNA sequence encoding a region of β -globin, and the primers are selected from the group consisting of primers SC1(+), SC2(-), SC3(+), SC4(-), SC5(+), SC6(-), SC-BA(-) and SC- BS(-).

36. (CANCELED)

37. (PREVIOUSLY PRESENTED) A composition comprising a replacement DNA fragment and a delivery vehicle suitable for delivery of the replacement DNA fragment into a cell containing a target fragment of a gene, wherein the replacement DNA fragment consists of:

- (a) at least one replacement exon having a 3' end and a 5' end;
- (b) a 3' end consisting of a 3' flanking noncoding sequence adjacent to the 3' end of the at least one replacement exon; and
- (c) a 5' end consisting of a 5' flanking noncoding sequence adjacent to the 5' end of the at least one replacement exon;

wherein the replacement DNA fragment includes less than all of the exons of the gene, wherein the delivery vehicle comprises a lipid, a dendrimer or polylysine, and wherein the 3' flanking noncoding sequence of the replacement DNA fragment is homologous to and anneals to a 3' flanking noncoding sequence adjacent to the target fragment, and the 5' flanking noncoding sequence of the replacement DNA fragment is homologous to and anneals to a 5' flanking noncoding sequence adjacent to the target fragment, so that the exogenous replacement DNA fragment replaces the target fragment of the gene upon delivery of the replacement DNA fragment into the cell.

38-40. (CANCELED)

41. (PREVIOUSLY PRESENTED) The method of claim 17, wherein the cell is a mammalian cell.

42. (PREVIOUSLY PRESENTED) The method of claim 41, wherein the mammalian cell is a human cell or a mouse cell.

43.-44. (CANCELED)